

## Original Article

# Changes in Aortic Wall Thickness at a Site of Entry Tear on Computed Tomography before Development of Acute Aortic Dissection

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**Objective:** To determine if there are changes in the aortic wall before acute aortic dissection (AD) that can be observed on contrast-enhanced computed tomography (CECT).

**Materials and Methods:** Twenty-two patients with AD who underwent CECT before developing AD were retrospectively identified and enrolled as the AD group. Twenty-five consecutive patients who underwent CECT and did not develop AD were enrolled as the control group. In the AD group, the site of entry tear was detected on CECT images; the aortic wall thickness at this site, defined as the dissection-related wall thickness (D-T), was then measured on CECT images acquired before AD. Moreover, the mean thickness of the ascending, thoracic descending, and abdominal aortic walls before AD was defined as the non-dissection-related wall thickness (non-D-T). In the control group, the aortic wall thickness was measured similarly and defined as the control wall thickness (C-T). The D-T, non-D-T, and C-T values were compared using one-way analysis of variance with the Games–Howell pairwise comparison test.

**Results:** The D-T ( $2.17 \pm 0.75$  mm) was significantly greater than the non-D-T ( $1.58 \pm 0.22$  mm;  $P < .01$ ) and C-T ( $1.53 \pm 0.15$  mm;  $P < .01$ ).

**Conclusion:** The aortic wall may have become thicker prior to the onset of AD.

**Keywords:** aneurysm, dissecting, aorta, X-ray

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## Introduction

Population-based studies suggest that the incidence of acute aortic dissection (AD) ranges from 2 to 16 cases per 100,000 person-years.<sup>1–3</sup> AD is relatively uncommon and often presents acutely as a catastrophic illness. Immediate mortality is approximately 40%, and perioperative mortality is 5%–20%; furthermore, 5-year survival after surgery ranges from 50% to 70%, depending on patient age and the underlying etiology.<sup>4–7</sup> Numerous risk factors for AD have been reported, including hypertension, aortic aneurysm, obstructive sleep apnea, bicuspid aortic valve, and genetic connective tissue disorders, such as Marfan syndrome, Loeys–Dietz syndrome, and Ehlers–Danlos syndrome.<sup>8–11</sup> Cystic medial necrosis, or the degeneration of the medial layer of the aorta, is thought to be a prerequisite for the development of AD. Blood passes into the aortic media through the tear, separating the intima from the surrounding media and/or adventitia and creating a false lumen.<sup>8,12</sup> However, the cause of AD remains unclear. To the best of our knowledge, no study has explained the changes in the aortic wall that occur before the development of AD using contrast-enhanced computed tomography (CECT). The aim of this study was to determine if there are changes in the aortic wall before acute AD that can be detected on CECT.

## Materials and Methods

The protocol for this retrospective study was approved by our institutional review board and was compliant with the Health Insurance Portability and Accountability Act. The requirement for written informed patient consent was waived (29-12-875).

## Classification of aortic dissection

We classified the type of AD according to whether there was blood flow in the false lumen as per the Japanese Circulation Society guideline<sup>13</sup>:

1. A non-communicating AD, defined as complete thrombo-

- sis of the false lumen without communication of blood flow between the true lumen and the false lumen
2. A non-communicating AD with an ulcer-like projection (ULP), defined by a focal, well-defined pouch of contrast medium measuring  $\leq 10$  mm in length on CECT and projecting into the non-communicating false lumen along the long axis of the aorta
  3. A communicating AD, defined by a pouch of contrast medium along the long axis of the aorta measuring  $>10$  mm in length on CECT, with communication of blood flow between the true lumen and the false lumen, as well as partial thrombosis of the false lumen and the absence of thrombosis in the true lumen

### Study population

Six hundred and fifty-nine patients were diagnosed to have AD on CECT at our hospital from October 2005 to September 2017. Twenty-five of these patients underwent CECT before developing AD. Two patients who underwent an ascending aortic replacement ( $n=1$ ) or abdominal aortic replacement ( $n=1$ ) and one patient who had an undetectable entry tear or ULP, which was considered a non-communicating AD, were excluded, leaving 22 patients for enrolment in the AD group. The median interval between the previous CECT and the CECT performed at the onset of AD was 527 (range 10–2,462) days. The AD group included nine men and 13 women of mean age  $75.7 \pm 10.0$  (range 50–92) years; 12 had a communicating AD, and 10 had a non-communicating AD with ULP. The Stanford classification was type A in nine patients and type B in 13 patients. The DeBakey classification was type I in three patients, type II in four patients, type IIIa in six patients, and type IIIb in nine patients. The indications for the earlier CECT were malignancy ( $n=9$ ), thoracic aortic aneurysm ( $n=6$ ), abdominal aortic aneurysm ( $n=2$ ), venous thrombosis ( $n=2$ ), trauma ( $n=2$ ), and thoracoabdominal aortic aneurysm ( $n=1$ ). No patient had a previous history or clinical symptoms of AD.

The control group consisted of 25 consecutive non-selected patients (12 men, 13 women; mean age  $75.2 \pm 7.0$  [range 52–85] years) without any history of AD who underwent CECT for reasons other than detection of AD in January 2011 and did not develop AD in the subsequent 527 days (the median follow-up duration in the AD group). The indication for CECT was malignancy in 24 patients and sarcoidosis in one patient. Patients who died of causes other than AD if the follow-up duration was less than 527 days were eligible for inclusion. Patients with aortic aneurysm were included but not those who underwent open aortic prosthetic reconstruction surgery or endovascular aortic repair. The median follow-up duration was 1,676 (range 111–3,400) days. Three patients died as a result of malignancy, and one died because of respiratory insufficien-

cy. There were no cases of genetic connective tissue disorder in either the study group or the control group.

### Computed tomography (CT) imaging

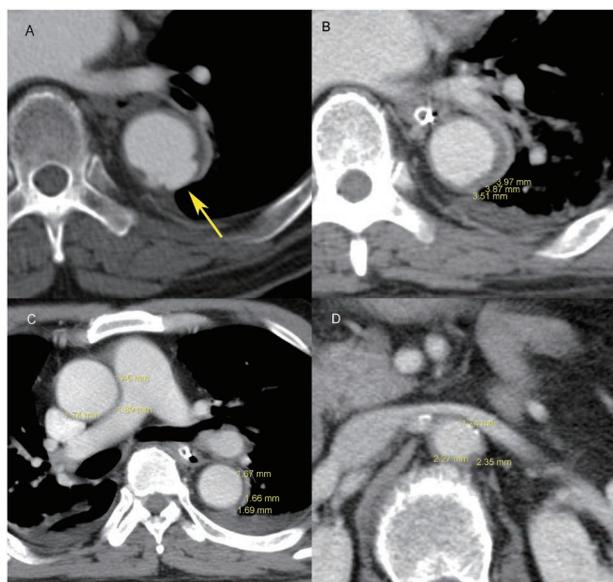
CT examinations were performed using a 320-row multidetector CT (MDCT) scanner (Aquilion ONE; Toshiba, Otawara, Japan), a 256-row MDCT scanner (Revolution CT; GE Healthcare Japan, Tokyo, Japan), a 64-row MDCT scanner (Optima CT 660 or LightSpeed VCT, GE Healthcare Japan; Scenaria; Hitachi, Tokyo, Japan), a 32-row MDCT scanner (LightSpeed VCT), or a 16-row MDCT scanner (Eclis, Hitachi).

The imaging parameters were as follows: tube voltage, 120 kV; tube current, 200–650 mA depending on body mass index; gantry rotation speed, 0.35–0.4 s/rotation depending on the CT scanner; collimation,  $64 \times 0.5$  mm; and helical pitch, 0.984. A contrast material with an iodine concentration of 350 mgI/mL (Iomeron; Eisai, Tokyo, Japan) was used. A  $540 \text{ mgI/kg} \times \text{body weight (kg)}$  dose of contrast medium was administered with an injection time of 30 s. Scan delay was determined by a computer-assisted bolus-tracking system. The arrival of the contrast medium was monitored, with a region of interest placed at the tracheal bifurcation level of the descending aorta. The trigger threshold was set at 200 Hounsfield units in the region of interest. Image acquisition commenced after triggering. Images were acquired during a single breath hold (head-to-foot direction) from the level of the sternal end of the clavicle to the groin. Helical data were reconstructed in the axial plane with a section thickness of 0.5 mm at intervals of 0.5 mm.

### Aortic wall thickness

Entry tears or ULPs before the onset of AD were initially detected on CECT by consensus between two radiologists. After detection of the entry tears or ULPs, each radiologist measured the aortic wall thickness independently and then calculated the mean values of the measurements obtained by both radiologists. Aortic walls with atherosclerosis or mural thrombus were included and those with calcification were excluded.

In the AD group, entry tears or ULPs were detected on CECT after the development of AD. The aortic wall thickness at the site of development of these entry tears or ULPs was measured three times on CECT images which were acquired before the development of AD. The mean of the three thickness measurements was recorded and defined as the dissection-related aortic wall thickness (D-T). The mean of the ascending, thoracic descending, and abdominal aortic wall thickness values before development of AD was also calculated and defined as non-dissection-related aortic wall thickness (non-D-T). **Figure 1** shows an example of a non-communicating AD with ULP. The aortic wall thickness was measured in the control group in the same



**Fig. 1** Axial computed tomography images showing a non-communicating AD with an ulcer-like projection in a 69-year-old male. **(A)** The image shows the onset of AD and a slice of the ulcer-like projection (arrow). **(B)** The image shows the same lesion on the aortic wall before the onset of AD and the wall thickness values at this site. The mean of these measurements is defined as D-T. **(C, D)** The image shows a slice of the ascending, thoracic descending, and abdominal aorta before the development of AD and the wall thickness values at each site. The mean of these measurements is defined as non-D-T.

AD: aortic dissection; D-T: dissection-related aortic wall thickness; non-D-T: non-dissection-related aortic wall thickness

way as for non-D-T, i.e., the thicknesses of the ascending, thoracic descending, and abdominal aortic walls were measured, and the mean value was defined as the control aortic wall thickness (C-T).

We then compared the D-T, non-D-T, and C-T values. Subgroup analysis was also performed in the AD group, whereby we compared the D-T in communicating ADs with that in non-communicating ADs with ULP.

### Statistical analysis

All statistical analyses were performed using SPSS version 19 for Windows (IBM Corp., Armonk, NY, USA). Summary statistics comparing the two groups are presented as the frequency for categorical variables and as the mean  $\pm$  standard deviation for continuous variables. Categorical variables were compared using the Chi-square test, and continuous variables were compared using the unpaired Student's t-test. Moreover, D-T, non-D-T, and C-T values were compared using one-way analysis of variance and application of the Games–Howell pairwise comparison test for multiple comparisons. A P-value  $< .05$  was considered statistically significant.

## Results

### Study population

Table 1 shows the demographics and clinical characteristics of the two study groups. Hypertension and aortic aneurysm were significantly more common in the AD group (17 and 9 patients) than in the control group (9 and 0 patients, respectively;  $P < .01$ ).

The demographics and clinical characteristics of patients with communicating ADs and those with non-communicating ADs and ULPs are shown in Table 2. Dyslipidemia was significantly more common in the group with non-communicating ADs and ULPs ( $P < .05$ ). There was also no significant difference in Stanford or DeBakey classification between the groups.

### Aortic wall thickness

In the AD group, the D-T was  $2.17 \pm 0.75$  mm, the non-D-T was  $1.58 \pm 0.22$  mm, and the C-T was  $1.53 \pm 0.15$  mm. The D-T was significantly greater than the non-D-T ( $P < .01$ ) and the C-T ( $P < .01$ ). There was no significant difference between the non-D-T and C-T values (Fig. 2). Moreover, the D-T was  $1.84 \pm 0.46$  mm in patients with communicating AD and  $2.57 \pm 0.87$  mm in those with non-communicating AD with ULP (Fig. 3); the D-T in patients with non-communicating AD with ULP was significantly greater than that in patients with communicating AD ( $P < .05$ ; Fig. 3).

## Discussion

In this study, the D-T was thicker than either the non-D-T or the C-T, indicating that an entry tear or ULP may occur if the aortic wall becomes thickened. The aortic wall consists of three layers, i.e., the intima, media, and adventitia. The media layer occupies the largest portion of the wall and contains lamellar units composed of elastic fibers, smooth muscle, collagen fibers, and a matrix; these components combine to form a rigid structure, allowing the aortic wall to withstand various stresses. Cystic medial necrosis, or degeneration of the aortic media, is thought to be a prerequisite for the development of AD.<sup>12,14–20</sup> Increased aortic wall thickness has been thought to originate from mural thrombus or a thickened intima, media, or adventitia. Arteriosclerosis, such as endothelial cell proliferation and atherosclerosis, leads to thickening of the aortic wall. The relationship between AD and atherosclerosis is unclear; however, it has been reported that atherosclerosis may be associated with AD in older adults.<sup>11</sup> Degeneration of the aortic media may lead to thickening of the aortic wall. Cystic medial necrosis has been implicated in the pathogenesis of AD and is a complex process that involves apoptosis and disarray of smooth muscle cells, destruc-

**Table 1** Patient characteristics in the acute AD and control groups

	AD group (n=22)	Control group (n=25)	P-value
Sex			0.63
Male	9	12	
Female	13	13	
Age (years)	75.7±10.0 (50–92)	75.2±7.0 (52–85)	0.84
Hypertension	17	9	<.01
Diabetes	3	3	0.87
Dyslipidemia	6	4	0.35
Hyperuricemia	3	0	0.06
Smoking	9	13	0.45
Aortic aneurysm	9	0	<.01
Stanford classification			
A	9		
B	13		
DeBaakey classification			
I	3		
II	4		
IIIa	6		
IIIb	9		
Development of blood flow in the false lumen			
Non-communicating	0		
Non-communicating with ULP	10		
Communicating	12		

AD: acute aortic dissection; ULP: ulcer-like projection

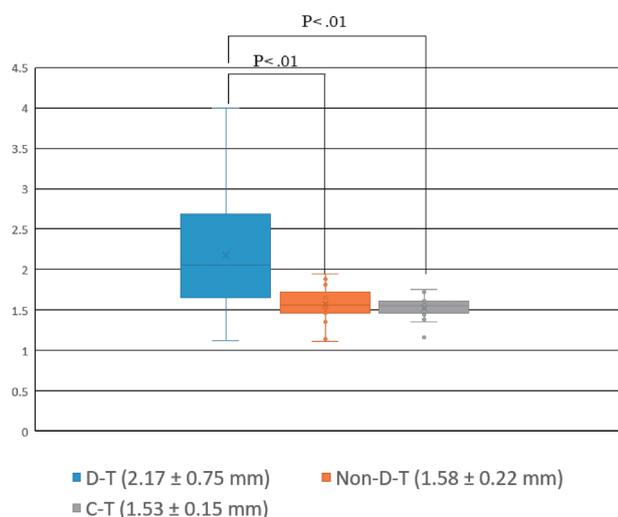
**Table 2** Characteristics of patients with communicating AD and those with non-communicating AD with ULP

	Communicating AD (n=12)	Non-communicating AD with ULP (n=10)	P-value
Sex			0.10
Male	3	6	
Female	9	4	
Age (y)	74.5±10.6 (50–89)	77.2±9.7 (64–92)	0.54
Hypertension	10	7	0.46
Diabetes	1	2	0.43
Dyslipidemia	1	5	0.02
Hyperuricemia	1	2	0.43
Smoking	4	5	0.43
Aortic aneurysm	6	3	0.30
Stanford classification			0.05
A	7	2	
B	5	8	
DeBaakey classification			0.12
I	2	1	
II	4	0	
IIIa	3	3	
IIIb	3	6	

AD: aortic dissection; ULP: ulcer-like projection

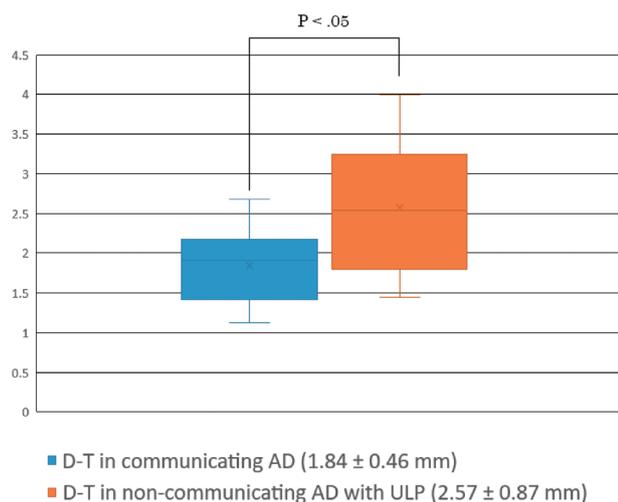
tion of elastic fibers, and accumulation of proteoglycans in the aortic media. There is growing evidence that many familial AD syndromes can be attributed to mutations in genes encoding contractile proteins. In patients with these mutations, typical histologic findings include degeneration

of the aortic media, with focal areas of increased smooth muscle cells and focal fibromuscular dysplasia of the vasa vasorum, which leads to narrowing of the lumen. In addition, there is an increased deposition of mucopolysaccharides in the extracellular matrix and hyperplasia of the



**Fig. 2** Aortic wall thickness where an entry tear or ulcer-like projection was present before the onset of AD. The D-T was  $2.17 \pm 0.75$  mm, the non-D-T was  $1.58 \pm 0.22$  mm, and the C-T was  $1.53 \pm 0.15$  mm. The D-T value was significantly higher than either the C-T value ( $P < .01$ ) or the non-D-T value ( $P < .01$ ).

AD: aortic dissection; C-T: control wall thickness; D-T: dissection-related wall thickness; non-D-T: non-dissection-related wall thickness



**Fig. 3** Aortic wall thickness where an entry tear or ULP was present before the onset of AD. The D-T was  $1.84 \pm 0.46$  mm in communicating AD and  $2.57 \pm 0.86$  mm in non-communicating AD with ULP. The D-T value in non-communicating AD was significantly higher than that in communicating AD ( $P < .05$ ).

AD: aortic dissection; D-T: dissection-related wall thickness; ULP: ulcer-like projection

smooth muscle cells in the aortic media, which may lead to diffuse thickening of the aortic wall.<sup>21-23</sup> Intramural hematoma may also be related to such thickening.

Recent studies have reported that severe atherosclerosis tends to increase the risk of non-communicating AD with

ULP.<sup>24</sup>) In the present study, the D-T in patients who had non-communicating AD with ULP was significantly greater than that in those with communicating AD. This result indicates that ULP may occur in an aortic wall with atherosclerosis in addition to the aortic wall changes related to the development of AD. However, when using CECT, it is difficult to distinguish between the components of the aortic wall and to detect any specific findings that suggest pathologic changes, such as density or contrast effect, due to spatial resolution issues.

There are some limitations to this study, in that it had a retrospective design, the patient population was small, and the observation period in the AD group was variable. Therefore, we cannot be certain that thickening of the aortic wall is definitely related to the onset of AD. Further studies involving a larger, more homogeneous population are needed in the future. However, we have confirmed that AD is preceded by changes in the aortic wall.

## Conclusion

In conclusion, our present findings suggest that, in patients with AD, the aortic wall at the site of the entry tear or ULP is thicker than that at other sites in the aortic wall. Therefore, the aortic wall may have become thicker prior to the onset of AD.

## Disclosure Statement

There are no conflicts of interest to declare.

## Author Contributions

Study design: HS, HH

Analysis: HS, TU, TM

Preparation of manuscript: HS

Interpretation of data: all authors

Critical review and revision: all authors

Final approval of the article: all authors

Accountability for all aspects of the work: all authors

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